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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/808,496	03/24/2004	Anuschirvan Peyman	446.016-DIV	5709
	7590 01/05/200 COSTIGAN P.C.	HYAMIN		
1185 AVENUE OF THE AMERICAS			TRUONG, TAMTHOM NGO	
NEW YORK, N	NY 10036		ART UNIT PAPER NUMBER	
			1624	
SHORTENED STATUTOR	Y PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE	
3 MONTHS • 01/05/2007 PAPE		PER		

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

	Application No.	Applicant(s)	
	10/808,496	PEYMAN ET AL.	
Office Action Summary	Examiner	Art Unit	
	Tamthom N. Truong	1624	
The MAILING DATE of this communication ap Period for Reply	opears on the cover sheet w	th the correspondence address	
A SHORTENED STATUTORY PERIOD FOR REPL WHICHEVER IS LONGER, FROM THE MAILING I - Extensions of time may be available under the provisions of 37 CFR 1 after SIX (6) MONTHS from the mailing date of this communication. - If NO period for reply is specified above, the maximum statutory period. - Failure to reply within the set or extended period for reply will, by statu Any reply received by the Office later than three months after the maili earned patent term adjustment. See 37 CFR 1.704(b).	DATE OF THIS COMMUNI.  136(a). In no event, however, may a did will apply and will expire SIX (6) MON te, cause the application to become Al	CATION: eply be timely filed ITHS from the mailing date of this communication. BANDONED (35 U.S.C. § 133).	
Status			
1)⊠ Responsive to communication(s) filed on <u>8-2</u> :	9-06 (RCE).	•	
	is action is non-final.		
3) Since this application is in condition for allows		ers, prosecution as to the merits is	
closed in accordance with the practice under	•	·	
Disposition of Claims			
4)⊠ Claim(s) <u>1-6,8 and 11</u> is/are pending in the a	onlication		
4a) Of the above claim(s) is/are withdra	•		
5)⊠ Claim(s) <u>1-6 and 8</u> is/are allowed.			
6)⊠ Claim(s) <u>11</u> is/are rejected.			
7) Claim(s) is/are objected to.			
8) Claim(s) are subject to restriction and/	or election requirement.		
Application Papers			
9) The specification is objected to by the Examin			
10) The drawing(s) filed on is/are: a) ac		•	
Applicant may not request that any objection to the	* * * * * * * * * * * * * * * * * * * *	` ,	
Replacement drawing sheet(s) including the correct			
11)☐ The oath or declaration is objected to by the E	examiner. Note the attached	Oπice Action or form P1O-152.	
Priority under 35 U.S.C. § 119	•		
<ul> <li>12) Acknowledgment is made of a claim for foreign a) All b) Some * c) None of:</li> <li>1. Certified copies of the priority document</li> <li>2. Certified copies of the priority document</li> <li>3. Copies of the certified copies of the priority application from the International Bureat</li> <li>* See the attached detailed Office action for a list</li> </ul>	ats have been received.  ats have been received in A  crity documents have been  au (PCT Rule 17.2(a)).	oplication No received in this National Stage	
Attachment(s)			
Notice of References Cited (PTO-892) Notice of Draftsperson's Patent Drawing Review (PTO-948) Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date	Paper No(s	ummary (PTO-413) )/Mail Date formal Patent Application 	

## Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8-29-06 has been entered.

Applicant's preliminary amendment has been fully considered. As stated in the previous actions, claim 11 was inadvertently included, but should have been withdrawn. However, since no art found for compound claims, claim 11 will be examined.

Claims 7, 9 and 10 have been cancelled.

Claims 1-6, 8 and 11 are pending.

## Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**Scope of Enablement:** Claim 11 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating osteoporosis using the claimed compounds does not reasonably provide enablement for a method of treating any bone

disorder using said compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

- (1) The breadth of the claims;
- (2) The amount of direction or guidance presented;
- (3) The state of the prior art;
- (4) The relative skill of those in the art;
- (5) The predictability or unpredictability of the art;
- (6) The quantity of experimentation necessary;

[See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also In re Wands, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The Breadth of the claims: Claim 11 recites: "A method of treating bone disorders in warm-blooded animals comprising administering to warm-blooded animals in need thereof an amount of the compound of claim 1 sufficient to treat bone disorders." The term "bone disorders" encompasses osteoporosis as well as arthritis and many others, see the following excerpt:

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[0237] Bone diseases for whose treatment and prevention the compounds of the formula I according to the invention can be employed are especially osteoporosis, hypercalcemia, osteopenia, for example caused by metastases, dental disorders, hyperparathyroidism, periarticular erosions in rheumatoid arthritis and Paget's disease. In addition, the compounds of the formula I can be used for the allevation, avoidance or therapy of bone disorders which are caused by a glucocorticoid, steroid or corticosteroid therapy or by a lack of sex hormone(s). All these disorders are characterized by bone loss which is based on the inequilibrium between bone formation and bone destruction and which can be favorably influenced by the inhibition of bone resorption by osteoclasts. The compounds of the formula I and/or their

Furthermore, formulae IIIa, IIIb and IIIc of claim 1 cover a myriad of compounds. Thus, the scope of claim 11 is not only broad in term of various bone disorders but also broad in term of a large number of compounds to select from.. Therefore, the scope of claim 11 is unduly broad.

The amount of direction or guidance presented: The specification describes a bioassay for the inhibition of vitronectin (Vn). Six compounds were tested for such an inhibition; however, they were all purine compounds. Although all tested compounds have naphthyridinyl-piperidine substituent just as those claimed herein, the purine portion distinguishes the test compounds from all those claimed herein. That is, the specification provides no adequate support for how to use **representative** scope of naphthyridinyl-piperidine

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claimed which can carry a variety of bicyclic rings as in formulae IIIa, IIIb and IIIc. Receptor binding is known to be structure-sensitive in general. Note **In re Surrey** 151 USPQ 724 regarding sufficiency of disclosure for a Markush group where as herein no examples of a diverse nature have been made much less tested to show the requisite activity needed to practice the invention. Also, see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as pharmaceutical art.

The state of the prior art: Currently, the state of the art reveals that vitronectin antagonists can inhibit osteoclast adhesion, and thus, inhibit bone resorption as evident by the article of Gowen et. al. The closest vitronectin antagonist is that of Merck, which has the naphthyridinyl-piperidine portion, but lacks the bicyclic portion as in the claimed formulae IIIa, IIIb and IIIc. Furthermore, the side effect profile of vitronectin antagonist has yet to be determined. The teaching of Gowen et. al. also does not relate the inhibition of vitronectin to other bone disorders such as those listed in the specification. Thus the state of the art does not support the broad scope of treatment using a myriad of compounds as claimed herein.

The relative skill of those in the art: Even with the advanced training, the skilled clinician would have to carry out extensive research to select an effective compound from the large Markush group of the three formulae claimed herein. Not only one has to determine an IC<sub>50</sub> value, but also *in-vivo* activity to establish an LD<sub>50</sub>, therapeutic index and pharmacokinetic

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profile for each compound. Given a large Markush group of the three claimed formulae, such a task would require a tremendous amount of effort, time and resource.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The pharmaceutical art has been known for its unpredictability due to various conflicting pathways, or biological factors that are sometimes genetically unique to individuals. In the instant case the claimed formulae IIIa, IIIb and IIIc do not have structural similarity with the tested compounds to warrant activity on vitronectin receptor, thus the skilled chemist would have to carry out undue experimentation to use compounds of the claimed formulae.

Note, the Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and use the full scope of the invention without 'undue experimentation".

## Allowable Subject Matter

Claims 1-6 and 8 are allowed as being drawn to compounds with the combination of naphyridinyl-(piperidinyl or cyclohexanyl)-(fused pyrimidine or pyridine) that are not taught or fairly suggested by the prior art of record.

## References on PTO-892

References cited on PTO-892 show state of the art only because they fail to teach the combination of rings as represented by the instant formulae IIIa, IIIb and IIIc.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M, T and Th (9:00-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Tamthom N. Truong

Examiner

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12-21-06

JAMES O. WILSON

SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600